The QT interval increases with decreasing plasma potassium in the Danish general population

Kanters, Jørgen K.; Graff, Claus; Henriksen, Lise; Petri, Anne Sofie; Christiansen, Michael; Nielsen, Jimmi; Kvetny, Jan; Ellervik, Christina

Publication date:
2015

Document Version
Accepted author manuscript, peer reviewed version

The QT interval increases with decreasing plasma potassium in the Danish general population

Jørgen K. Kanters[1,7], Claus Graff[2], Lise Henriksen[1], Anne Sofie Petri[1], Michael Christiansen[3], Jimmi Nielsen[4], Jan Kvetny[5], Christina Ellervik[6]

[1]Laboratory of Experimental Cardiology, University of Copenhagen, Denmark, [2]Department of Health Science and Technology, Aalborg University, Denmark, [3]Statens Seruminstitut, Copenhagen, Denmark, [4]Department of Clinical Medicine, Aalborg Psychiatric Hospital, Aalborg, Denmark, [5]Dept. of Clinical Biochemistry, Naestved Sygehus, Denmark, [6]Department of Laboratory Medicine, Boston Children's Hospital, Boston, MA, USA, [7]Department of Cardiology, Herlev & Gentofte University Hospital, Copenhagen, Denmark.

It is a well-known fact that during hypokalemia, the corrected QT interval prolongs and the T-waves flattens and may even get humps, During hyperkalemia the corrected QT interval shortens and T-waves get higher amplitudes and become more peaked. However the magnitude of these repolarization changes during physiological variations of Se-K is unknown.

Methods

Subjects were enrolled from the Danish General Suburban Population Study (GESUS). GESUS is a cross-sectional study of the adult suburban general population in Naestved municipality (70 km south of Copenhagen) initiated in January 2010.
The Full Cohort of participants having an electrocardiogram (ECG) recorded consisted of 9914 subjects.
The (assumed) Healthy group excluded participants with self-reported history of myocardial infarction/angina pectoris, history of cerebrovascular incident, diabetes mellitus, Hba1c>42, estimated glomerular filtration rate lower than gender- and age-adjusted 5% percentile, intake of any cardiac medicamentation including diuretics, diabetes or insulin injections, consisted of 6314 patients.

ECGs were recorded on a digital ECG recorder (MAC5000, GE-Medical Systems, Milwaukee, WI, USA), at a sampling rate of 500 Hz. Each 10-second ECG was used to form a median beat in the recorded leads using MUSE/Interval Editor software (GE Health care, Milwaukee, WI, USA), where representative beat waveforms were constructed for each lead after baseline removal and then superimposed to construct a superlead. QT measurements were made automatically using the 12SL-algorithm (12SL, GE-Medical Systems, Milwaukee, WI, USA). QT intervals were corrected for heart rate with Fridericia's formula (QTcF =(QT/RR)$^{1/3}$).

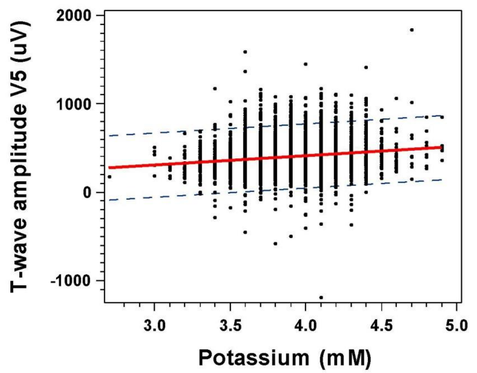
Results

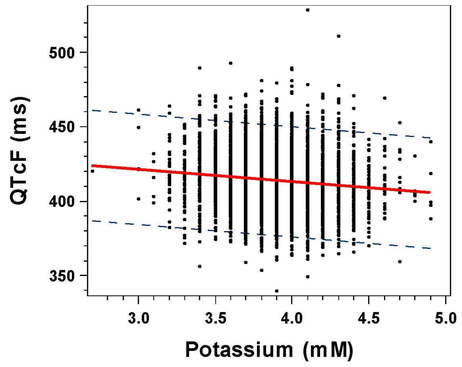
Mean±SD		Full Cohort	Assumed Non-Healthy	Assumed Healthy
Demographics				
n		8779	3438	5341
age	y	56.45±13.53	64.11±11.62*	51.52±12.32
male	%	45.8%	47.1% (p=0.052)	45.0%
ECG parameters				
QTcF	ms	416.5±20.4	420.5±21.8*	413.9±19.0
QTcB	ms	420.9±24.5	427.7±25.2*	416.4±22.9
RR	ms	956.0±163.9	918.6±159.8*	980.2±162.0
Clinical Chemistry				
Se-Potassium	mM	3.883±0.297	3.894±0.342*	3.876±0.264
Se-Sodium	mM	140.70±2.24	140.52±2.52*	140.82±2.03
Creatinine	µM	77.39±19.42	80.94±25.45*	75.14±13.83

Demographics of the Assumed healthy GESUS population. *p<0.05 vs. Healthy

QTcF (ms)	Univariate α	95% CI	Multivariate α	95% CI
age (y)	0.21*	[0.17; 0.25]	0.26*	[0.21; 0.30]
gender (M vs. F)	-7.4*	[-8.4;-6.4]	-6.7*	[-7.7; -5.7]
Se-Potassium (mM)	-8.4*	[-10.3;-6.4]	-8.3*	[-10.2;-6.3]
Se-Sodium (mM)	0.12	[-0.12; 0.38]		
Creatinine (µM)	-0.17	[-0.21; -0.14]		
Intercept			436*	[429; 443]
T-wave Amplitude V5 (µV)				
age (y)	-1.8*	[-2.2; -1.4]	-2.3*	[-2.7; -1.9]
gender (M vs. F)	100*	[90;110]	83*	[95; 120]
Se-Potassium (mM)	103*	[85;123]	83*	[77;115]
Se-Sodium (mM)	-0.09	[-2.6; 1.2]		
Creatinine (µM)	2.0*	[1.6; 2.4]	-0.9*	[-1.4;-0.5]
Intercept			161*	[85; 236]

Univariate and Multivariate linear regression of QTcF and T-wave amplitude in lead V5 (Assumed healthy GESUS population). *p<0.05





Conclusion

- T-wave amplitude decreases **103 µV per mM** decrease in potassium
- QTcF interval increases with **8.4 ms per mM** decrease in potassium
- Since FDA has a threshold of concern of ΔQTc=5 ms, it seems necessary to take plasma levels of potassium into account when analyzing data in studies with drug-induced repolarization changes